

REMARKS/ARGUMENTS

Reconsideration is respectfully requested. Claims 11-25 are pending in the application. Claims 14-16 and 19 are withdrawn from consideration. Amendment to and withdrawal of the claims do not affect inventorship.

Applicant has not dedicated nor abandoned any unclaimed subject matter. Moreover, Applicant has not acquiesced to any rejections or objections made by the Patent Office. Applicant reserves the right to pursue prosecution of any presently excluded claim embodiments in future continuation and/or divisional applications.

In the Specification

The specification has been amended to delete reference to U.S. Patent No. 7,090,804 and replace it with reference to U.S. Application No. 09/135,183, which was referenced in the application as filed. Applicants submit that No New Matter is introduced by way of this

Claims Rejections Under 35 USC §112

Claims 11-13, 17-18 and 20-25 are pending and stand rejected as allegedly failing to comply with the written description (first paragraph) and definiteness requirements (second paragraph) of 35 USC §112. Specifically at issue are the claim phrases, “the input waveform eliciting a response of characteristic waveform that is unique to the target analyte signals...” (claim 11) and “receiving an output waveform that is unique to target analyte signals from the electrode, responsive to the input waveform” (claim 25).

As authority, the Examiner cites MPEP 2163.06, which states in part, “[T]he fundamental factual inquiry is whether a claim defines an invention that is clearly conveyed to those skilled in the art at the time the application was filed.” The same section emphasizes that the *whole* of the specification needs to be considered, not just select parts.

While the Examiner correctly notes that page 103 of the application states “[But] when correlated together, the data_{final} can have a characteristic response that is unique to target analyte signals” and “[A] characteristic curve of the peak information means a positive” (see ¶¶ [0439],

[0448] of US20040146909), one of skill in the art would understand the relationship of waveforms, electrodes and electron transfer based on the specification at the time the application was filed..

The application repeatedly references voltammetric and spectrographic procedures, each of which connotes to the person of skill in the art the use of waveforms. See, e.g., “Results” (¶¶ [0555] et seq. Moreover, one of skill in the art at the time of the application would recognize that energy occurs or can be measured by waveforms. For example, submitted herewith are pages from “Electrochemical Methods” which describe basic electrode techniques.¹ As described herein, the voltammetric methods refer to the waveforms applied in the experiments and depicted in the figures. Thus, one of skill in the art would appreciate that the *very definition* of voltammetry involves the measurement of energy required to initiate electron transfer between donor and accepting molecules, at least one of which is typically affiliated with an electrode surface.

The background section of the application reinforces this point, wherein is noted both input and output waveforms in connection with electron transfer and electrochemical detection in general:

[0006] In the area of electrochemical sensing, there are a number of electrochemical techniques that have been employed. Traditionally, electrochemical methods generally improve their signal to noise ratios by discriminating the faradaic signal from the background components in the time domain **through the application of pulsed waveforms**, i.e. differential pulse polarography and square wave **voltammetry**. Pulse methods are able to discriminate the faradaic current from the changing current in the time domain. Changing currents decay much more rapidly than faradaic current, i.e. exponentially as compared the inverse square root. Similarly, modulation techniques have also been used to improve signal to noise ratios; these methods utilize **the imposition of a modulated carrier wave (sine wave) on the signal**.

[0007] The frequency domain has only been used in a few electrochemical techniques to enhance the signal to noise ratio. In AC voltammetry, a potential ramp is applied to the electrode, and **a small amplitude sine wave is superimposed on the linear ramp**. However, the use of **large amplitude sinusoidal voltammetry in conjunction with the detection at higher harmonic frequencies using Fourier transforms has proven to be a**

¹ Appendix A: *Electrochemical Methods*; Bard and Faulkner, 1980 John Wiley & Sons (pp. 136-139 attached).

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useful method. See U.S. Pat. No. 5,650,061; Singhai et al., Anal. Chem. 69:1552 (1997); Singhal and Kuhr, Anal. Chem. 69:4828 (1997); Singhal et al., Anal. Chem. 69:3553 (1997); and Dontha et al., Anal. Chem. 69:2619 (1997), all of which are expressly incorporated by reference herein. (US20040146909; emphasis added).

The use of input and output waveforms is therefore clear to the person of ordinary skill in the art viewing the specification. Additionally, Applicants note that there is no *in haec verba* requirement whereby language used in the claims must appear verbatim in the specification.

Accordingly, for the foregoing reasons the rejection is respectfully deemed to be incorrect and asked to be withdrawn.

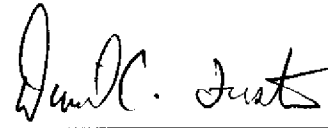
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CONCLUSION

In view of the foregoing amendments and arguments, Applicants believe all claims now pending in this application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned attorney, David Foster, at 415-442-1216.

Respectfully submitted,



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ELECTROCHEMICAL METHODS

Fundamentals and Applications

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John Wiley & Sons

New York • Chichester • Brisbane • Toronto • Singapore

Prefa

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chapter 5

Controlled Potential Microelectrode Techniques— Potential Step Methods

The next two chapters are concerned with methods in which the working electrode potential is forced to adhere to a known program. It may be constant or it may vary with time in a predetermined manner, and the current is measured as a function of time or potential. In the methods covered in the next five chapters, the electrode is a microelectrode, and the solution volume is large enough that the passage of current does not alter the bulk concentrations of electroactive species. Such circumstances are known as *small A/V conditions*. In this chapter, we will consider systems in which the mass transport of electroactive species occurs only by diffusion. Also, we will restrict our view for the moment to methods involving perturbations of the working electrode by step-functional changes in its potential. This family of techniques is probably the largest single group, and it contains some of the most powerful experimental approaches available to electrochemistry.

5.1 OVERVIEW OF STEP EXPERIMENTS

5.1.1 Types of Techniques

Figure 5.1.1 is a picture of the basic experimental system. An instrument known as a *potentiostat* has control of the voltage across the working electrode-counter electrode pair, and it adjusts this voltage in order to maintain the potential difference between the working and reference electrodes (which it senses through a high-impedance feedback loop) in accord with the program supplied by a function generator. One can view the potentiostat alternatively as an active element whose job is to force through the working electrode whatever current is required to achieve the desired potential at any time. Since the current and the potential are related functionally, that current is

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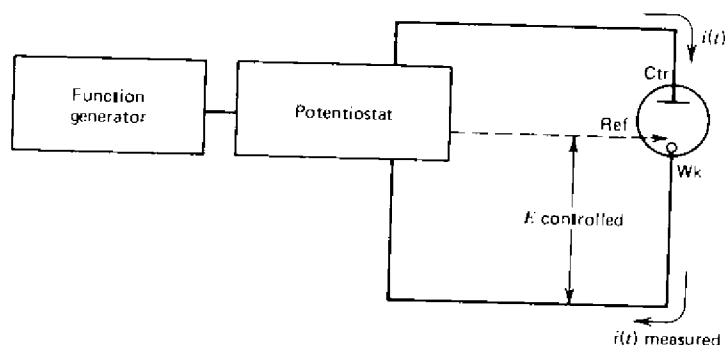


Figure 5.1.1
Schematic experimental arrangement for controlled potential experiments.

unique. Thus the potentiostat's response (the current) actually is the experimental observable. For an introduction to the design of such apparatus, see Chapter 13.

Figure 5.1.2a is a diagram of the waveform applied in a basic potential step experiment. Let us consider its effect on the interface between a solid electrode and an unstirred solution containing an electroactive species. As an example, take anthracene in deoxygenated DMF. We know that there generally is a potential region where faradaic processes do not occur; let E_1 be in this region. On the other hand, we can also find a potential at which the kinetics for reduction of anthracene become so rapid that no anthracene can coexist with the electrode, and its surface concentration goes

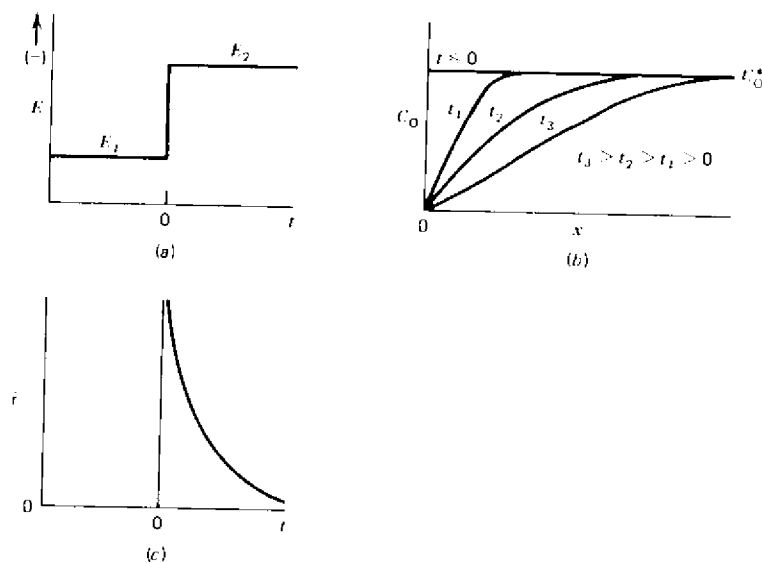


Figure 5.1.2

(a) Waveform for a step experiment in which species O is electroinactive at E_1 but is reduced at a diffusion-limited rate at E_2 . (b) Concentration profiles for various times into the experiment. (c) Current flow versus time.

nearly to zero. Consider E_2 to be in this "mass transfer limited" region. What is the response of the system to the step perturbation?

First, the electrode must instantly reduce the anthracene nearby to the stable anion radical:



This act requires a very large current, but subsequently current is required only because the reduction has created a concentration gradient that produces, in turn, a net flux of anthracene to the electrode surface. Since this material cannot coexist with the electrode at E_2 , it must be eliminated by reduction. The flux of anthracene, hence the current as well, is proportional to the concentration gradient at the electrode surface. Note, however, that the continued anthracene flux causes the zone of anthracene depletion to thicken; thus the slope of the concentration profile at the surface declines with time, and so does the current. Both of these effects are depicted in Figures 5.1.2b and 5.1.2c. This kind of experiment is called *chronoamperometry*, because current is recorded as a function of time.

Suppose we now consider a series of step experiments in the anthracene solution discussed above. Between each experiment the solution is stirred, so that the initial conditions are always the same. Similarly, the initial potential (before the step) is chosen to be at a constant value where no faradaic processes occur. The change from experiment to experiment is in the step potential, as depicted in Figure 5.1.3a. Suppose further that experiment 1 involves a step to a potential at which anthracene is not yet electroactive; that experiments 2 and 3 involve potentials where anthracene is reduced, but not so effectively that its surface concentration is zero; and that 4 and 5 have step

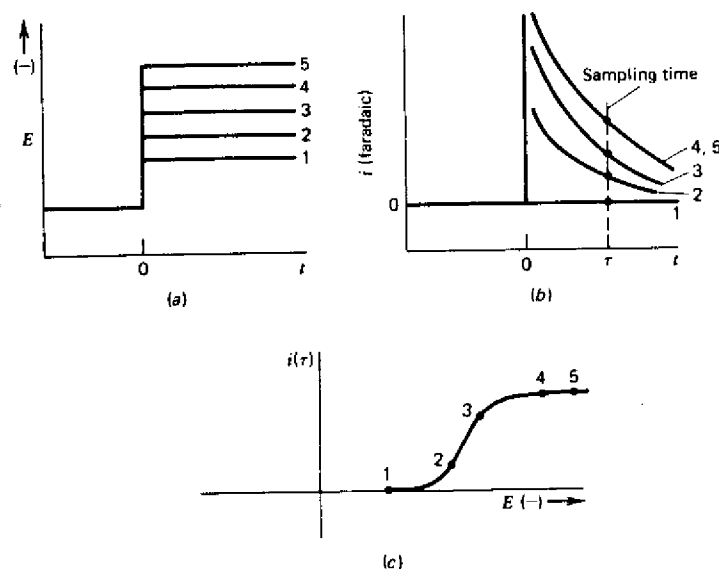


Figure 5.1.3

Sampled-current voltammetry. (a) Step waveforms applied in a series of experiments. (b) Current-time curves observed in response to the steps. (c) Sampled-current voltammogram.

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potentials in the mass-transfer-limited region. Obviously experiment 1 yields no faradaic current, and experiments 4 and 5 yield the same current we obtained in the chronoamperometric case above. In both 4 and 5, the surface concentration is zero; hence anthracene arrives as fast as diffusion can bring it, and the current is limited by this factor. Once the electrode potential becomes so extreme that this condition applies, the potential no longer influences the electrolytic current. In experiments 2 and 3 the story is different because the reduction process is not so dominant that some anthracene cannot coexist with the electrode. Still, its concentration is less than the bulk value, so anthracene does diffuse to the surface where it must be eliminated by reduction. Since the difference between the bulk and surface concentrations is smaller than in the mass-transfer-limited case, less material arrives at the surface per unit time, and the currents (for corresponding times) are smaller than in experiments 4 and 5. Nonetheless, the depletion effect still applies, which means that the current still decays with time.

Now suppose we sample the current at some fixed time τ into each of these step experiments; then we can plot the sampled current $i(\tau)$ vs. the potential to which the step takes place. As shown in Figures 5.1.3b and 5.1.3c, the current-potential curve has a waveshape much like that encountered in earlier considerations of steady-state voltammetry (Chapter 1) under convective conditions. This kind of experiment is called *sampled-current voltammetry*, and we will see that it really is the basis for *dc polarography* (voltammetry at the dropping mercury electrode) as well as the newer pulse polarographic methods.

Now consider the effect of the potential program displayed in Figure 5.1.4a. The forward step, that is, the transition from E_1 to E_2 at $t = 0$, is exactly the experiment that we have just discussed. For a period τ , it causes a buildup of the reduction product (e.g., anthracene anion radical) in the region near the electrode.

However, in the second phase of the experiment, after $t = \tau$, the potential returns to E_1 , where only the oxidized form (e.g., anthracene) is stable at the electrode. The anion radical cannot coexist there; hence a large anodic current flows as it begins to reoxidize, then the current declines in magnitude (Figure 5.1.4b) as the depletion effect sets in.

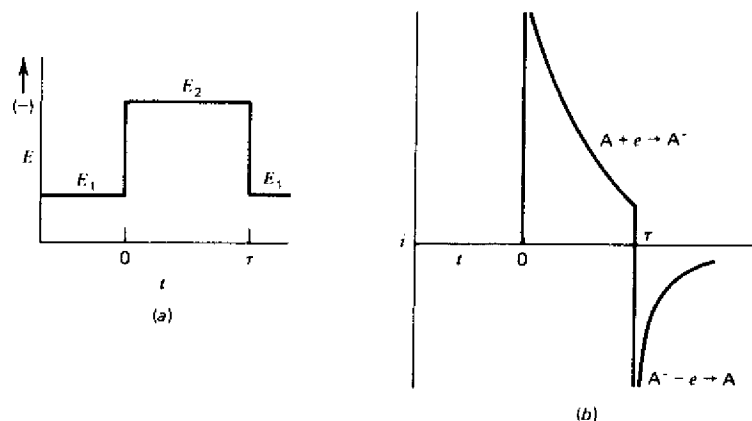


Figure 5.1.4

Double potential step chronoamperometry. (a) Typical waveform. (b) Current response.